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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/529,028	03/24/2005	Sarina Striem	800.1019	9002

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EXAMINER	
OH, TAYLOR V	

ART UNIT	PAPER NUMBER
1625	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/529,028	STRIEM ET AL.	
	Examiner	Art Unit	
	Taylor Victor Oh	1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 June 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *32-46* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *32-46* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *24 March 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Final Rejection

The Status of Claims

Claims 32-46 are pending.

Claims 32-46 are rejected.

Objection

The amendment filed 06/26/09 is objected to under 35 U.S.C. 132 because it introduces new matter into the disclosure. 35 U.S.C. 132 states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows: claim 32 has been amended to introduce the phrase "as compared to the control level of metalloproteinase (MMP) or calpain found in a normal mammal ", which does not have any literal support in the specification as filed. A close inspection of the original claims and specification do not provide antecedent basis for the proposed changes. New matter can not be introduced into specification at any time during the prosecution, unless there is a supporting description that would support the proposed changes. Applicant is required to cancel the new matter in the reply to this Office Action.

Claim Rejections - 35 USC § 112

Applicants' argument filed 6/26/09 have been fully considered but are not

persuasive.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The rejection of Claims 32-46 under 35 U.S.C. 112, first paragraph, has been maintained due to the lack in the scope of enablement requirement in inflammatory diseases, autoimmune diseases and cancer.

Even with the modification o f the claims, there are some other issues to be resolved in the followings:

Claims 32-46 rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

In claim 32, the phrase "as compared to the control level of metalloproteinase (MMP) or calpain found in a normal mammal " is recited. The phrase does not have any literal support in the specification as filed. A close inspection of the original claims and specification do not provide antecedent basis for the proposed changes. New matter can not be introduced into specification at any time during the prosecution, unless there is a supporting description that would support the proposed changes. Applicant is required to cancel the new matter in the reply to this Office Action.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 32-34,38-4043,45-46 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim 32, the phrase" a method for treating or managing a disease associated with an elevated metalloproteinase (MMP) or calpain in a mammal as compared to the control level of metalloproteinase (MMP) or calpain found in a normal mammal " is recited. This particular expression of the phrase" a disease associated with an elevated metalloproteinase (MMP) or calpain in a mammal" is vague and indefinite because of its reach-through claim. The claims do read on the future treatment of some disease associated with an elevated metalloproteinase (MMP) or calpain, which has not discovered yet. In order to overcome this rejection, the examiner recommends to add the specific diseases to the claims. Therefore, an appropriate correction is required.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The rejection of Claims 32-39,44-46 under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Kozak et al (WO99/16741) has been maintained

The rejection of Claims 32-39,44-46 under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Kozak et al (WO99/16741) has been maintained with the reason of record filed on 3/20/09.

Applicants' Argument

Applicants argue the following issues:

a. It is well established that elevated expression of MMP-9 is associated with tumor proliferation and in particular with pathogenic mechanisms in cancer ; also MMP-9 may be a rational target useful in the treatment of many types of cancer as shown in paragraphs [0066] to [0070] and examples 3 and 4; therefore, there is no problem with the scope of enablement issues ;

b. In examples 3, 8 and 9, diesters of BAPTA inhibit both basal and TNF-alpha-induced MMP activity; as tumor necrosis factor alpha is a pro-inflammatory cytokine and as MMP-9 is highly expressed as sites of inflammation and contributes to the pathogenesis of inflammatory diseases, any inflammation or inflammatory disease or disorder associated with an elevated MMP or calpain , which is mediated by the cytokine TNF-alpha, can be treated; thus, it is enabled;

c. The prior art does not teach or suggest the effect of DP-BAPTA molecules on activity of specific enzymes and the use of those compounds for the treatment of MMP and calpain related diseases and disorders;

d. The prior art does not have any teaching or suggestion for the cellular target affected by these chelators mentioned in the prior art ;

e. The prior art is directed to the treatment of conditions and diseases related elevated levels of divalent metal ions unlike the claimed invention which is directed to the use of those lipophilic diesters of the chelating agent for treating conditions and diseases associated with an elevated metalloproteinase or calpain in a mammal via its inhibition.

Applicants' arguments have been noted, but the arguments are not persuasive.

First, regarding the first argument, the Examiner has noted applicants' arguments. However, the claim sets forth the treatment of cancer generally. However, there never has been a compound capable of treating cancer generally. There are compounds that treat a range of cancers, but no one has ever been able to figure out how to get a compound to be effective against tumors generally, or even a majority of tumors. Thus, the existence of such a "silver bullet" is contrary to our present understanding in oncology. Even the most broadly effective antitumor agents are only effective against a small fraction of the vast number of different cancers known. This is true in part because cancers arise from a wide variety of sources, such as viruses (e.g. EBV, HHV-8, and HTLV-1), exposure to chemicals such as tobacco tars, genetic disorders, ionizing radiation, and a wide variety of failures of the body's cell growth regulatory mechanisms. Different types of cancers affect different organs and have different methods of growth and harm to the body, and different vulnerabilities. Thus, it is beyond the skill of oncologists today to get an agent to be effective against cancers generally, evidence that the level of skill in this art is low relative to the difficulty of such a task. Therefore, applicants argument about the treatment of caner in general by means of inhibiting the mechanism of MMP only is premature and is not persuasive.

Second, regarding the second argument, the Examiner has noted applicants' arguments. However, for a compound or genus to be effective against inflammation generally is contrary to medical science. Inflammation is a process which can take place in virtually any part of the body. There is a vast range of forms that it can take, causes

for the problem, and biochemical pathways that mediate the inflammatory reaction. There is no common mechanism by which all, or even most, inflammations arise. Mediators include bradykinin, serotonin, C3a, C5a, histamine, assorted leukotrienes and cytokines, and many, many others. Accordingly, treatments for inflammation are normally tailored to the particular type of inflammation present, as there is no, and there can be no "magic bullet" against inflammation generally.

Inflammation is the reaction of vascularized tissue to local injury; it is the name given to the stereotyped ways tissues respond to noxious stimuli. These occur in two fundamentally different types. Acute inflammation is the response to recent or continuing injury. The principal features are dilatation and leaking of vessels, and recruitment of circulating neutrophils. Chronic inflammation or "late-phase inflammation" is a response to prolonged problems, orchestrated by T-helper lymphocytes. It may feature recruitment and activation of T- and B-lymphocytes, macrophages, eosinophils, and/or fibroblasts. The hallmark of chronic inflammation is infiltration of tissue with mononuclear inflammatory cells. Granulomas are seen in certain chronic inflammation situations. They are clusters of macrophages which have stuck tightly together, typically to wall something off. Granulomas can form with foreign bodies such as aspirated food, toxocara, silicone injections, and splinters.
Otitis media is an inflammation of the lining of the middle ear and is commonly caused by Streptococcus pneumoniae and Haemophilus influenzae. Cystitis is an inflammation of the bladder, usually caused by bacteria. Blepharitis is a chronic inflammation of the eyelids that is caused by a staphylococcus. Dacryocystitis is inflammation of the tear

sac, and usually occurs after a long-term obstruction of the nasolacrimal duct and is caused by staphylococci or streptococci. Preseptal cellulitis is inflammation of the tissues around the eye, and Orbital cellulitis is an inflammatory process involving the layer of tissue that separates the eye itself from the eyelid. These life-threatening infections usually arise from staphylococcus. Hence, these types of inflammations are treated with antibiotics. Certain types of anti-inflammatory agents, such as non-steroidal anti-inflammatory medications (Ibuprofen and naproxen) along with muscle relaxants can be used in the non-bacterial cases. The above list is by no means complete, but demonstrates the extraordinary breadth of causes, mechanisms and treatment (or lack thereof) for inflammation. It establishes that it is not reasonable to any agent to be able to treat inflammation generally. Thus, the only pathogenesis of inflammatory diseases associated with an elevated MMP or calpain can not be applicable to the enablement for the scope of " all inflammation diseases" generally, which is not present in the specification .

Third, regarding the third through the fifth arguments, the Examiner has noted applicants' arguments. However, regardless of lacking in mentioning the mechanistic nature of inhibiting matrix metalloproteinase enzymes other than the elevated divalent metal ion the treatment in the prior art, the end result is still the same treatment for the same diseases of the claimed invention as described in the prior art (see page 12 ,lines 3-10). Moreover, they are identical with each other concerning their corresponding chemical formula. Therefore, it would have been obvious to the skilled artisan in the art

to be motivated to research and discover the role of the mechanistic nature of inhibiting effect of the prior art compound on the matrix metalloproteinase enzyme in an alternative pursuit for treating those claimed diseases by a routine experimentation.

Therefore, applicants' argument is not persuasive.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Taylor Victor Oh whose telephone number is 571-272-0689. The examiner can normally be reached on 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet Andres can be reached on 571-272-0867. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Taylor Victor Oh/
Primary Examiner, Art Unit 1625

11/04/09